

In the Claims:

1 – 86. (Canceled).

87. (Currently Amended) A method of regulating an activity of a SMAD protein in a mesenchymal stem cell (MSC), the method comprising contacting the ~~cell~~ MSC in vitro with an polynucleotide agent which is specifically hybridizable with TAK1 in the cell and/or an agent capable of suppressing an interaction of TAK1 with an MH2 domain of the SMAD protein, said agent being selected from the group consisting of a polypeptide encoded by a nucleic acid having a nucleotide sequence as set forth in SEQ ID NO: 1 and/or 2, a homolog having an amino acid sequence at least 70 % homologous to said polypeptide, a polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO: 1 and/or 2 and a polynucleotide comprising a nucleotide sequence encoding said homolog, wherein said TAK1 is encoded by a polynucleotide sequence as set forth in SEQ ID NO: 11, ~~agent capable of diminishing or abrogating an expression and/or an activity of TAK1 (Genbank Accession number: NM_145331, SEQ ID NO: 11) in the cell,~~ thereby regulating the activity of the SMAD protein in the mesenchymal stem cell.

88 – 89. (Cancelled)

90. (Currently Amended) The method of claim 87, wherein said agent ~~comprises a single stranded or double stranded oligonucleotide which is at least 12 nucleotides in length which and~~ is specifically hybridizable with said TAK1 ~~(Genbank Accession number: NM_145331, SEQ ID NO: 11).~~ comprises a single-stranded or double-stranded oligonucleotide which is at least 12 nucleotides in length.

91 – 93. (Cancelled)

94. (Currently Amended) A method of regulating osteogenesis and/or bone repair in a subject in need thereof, the method comprising:

(a) contacting in-vitro a mesenchymal stem cell with osteogenic potential with ~~a polynucleotide~~ an agent capable of modulating down-regulating an expression of

TAK1 in the cell and/or a polynucleotide or polypeptide agent capable of down-regulating an activity of TAK1 (Genbank Accession number: NM_145331, SEQ ID NO: 11) in the cell, wherein said TAK1 is encoded by a polynucleotide sequence as set forth in SEQ ID NO: 11, and wherein said activity of TAK1 is an interaction with an MH2 domain of a SMAD 2 protein, to generate a treated cell; and

- (i) ~~said cell is located in the subject; and/or~~
- (ii) ~~said contacting is effected in vitro, thereby generating a treated cell, and the method further comprises the step of (b) administering said treated cell to a bone of the subject, thereby regulating osteogenesis in the subject.~~

95 – 96. (Cancelled)

97. (Currently Amended) The method of claim 94, wherein said agent comprises a single-stranded or double-stranded oligonucleotide which is at least 12 nucleotides in length and is specifically hybridizable with said TAK1 (~~Genbank Accession number: NM_145331, SEQ ID NO: 11~~).

98 – 100. (Cancelled)

101. (Previously Presented) The method of claim 94, wherein the subject suffers from a disease selected from the group consisting of inflammation-mediated bone loss, periodontal disease, osteoarthritis, Kohler's bone disease, rheumatoid arthritis and osteoporosis.

102. (Currently Amended) The method of claim 94, with said agent capable of down-regulating an activity of TAK1 is selected from the group consisting of a polypeptide encoded by a nucleic acid having a nucleotide sequence as set forth in SEQ ID NO: 1 and/or 2, a homolog having an amino acid sequence at least 70 % homologous to said polypeptide, a polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO: 1 and/or 2 and a polynucleotide comprising a nucleotide sequence encoding said homolog, said agent being capable of suppressing wherein said activity of TAK1 is a kinase activity and/or an interaction of TAK1 with an MH2 domain of a SMAD-2 protein.

103 – 111. (Cancelled)

112. (Previously Presented)
is set forth in SEQ ID NO: 3.

The method of claim 87, wherein said agent

113. (Previously Presented)
is set forth in SEQ ID NO: 3.

The method of claim 94, wherein said agent